REMARKS

The present remarks address the substance of the Office Action.

"The drawings are objected to"

The Examiner objected to the drawings. The drawings on file are informal. Thus, formal drawings are attached.

"Claim 5 is objected to"

The Examiner objected to Claim 5 on the basis of certain informalities. The claim seems backwards. Claim 5 has been canceled.

"enabling for immunogenic compositions"

The Examiner rejected Claims 1-10 under 35 USC 112, first paragraph, on the basis that the specification, while being enabling for immunogenic compositions, does not provide enablement for a vaccine or other pharmaceutical composition, these latter requiring proof of protection. Correction was required. Amended Claims 1-10 recite "immunogenic compositions."

patentable over "Murphy T.F. (U.S. Patent Numbers 5,712,118 and 5,725,862), in view of Chen, D. et al (Infection and Immunity, Vol. 64, No. 6, pp. 1900-1905) and further in view of Gu et al. (U.S. Patent Number 6,207,157)"

The Examiner rejected Claims 1-10 under 35 USC 103(a) as being unpatentable over this combination of references. MPEP 706.02(j) requires that to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references when combined must teach or suggest all the claim limitations. Here, the three basic criteria are not met.

Murphy is said to teach a vaccine for *Moraxella catarrhalis* from a surface component protein "CD." Chen is said to teach evaluation of another surface component protein, ubiquitous surface protein A (UspA), from *Moraxella catarrhalis* for use as a vaccine. Major studies were said to have been done on the LOS of *Neisseria meningitidis* (Gu et al, Infection and Immunity, Vol. 61, No. 5, pp. 1873-1880, May 1993), and *Haemophilus influenzae* (Gu et al, Infection and Immunity, Vol. 63, No. 10,

pp 4115-4120, Oct 1995; Gu et al. Infection and Immunity, Vol. 64, No. 10, pp 4047-4053, Oct 1996; and Gu et al, Infection and Immunity, Vol. 65, No. 11, pp 4488-4493, Nov 1997) as potential vaccines. The Gu patent is said to teach the LOS of *Haemophilus influenzae* for use as a vaccine.

Starting with the last point first, that the prior art references when combined must teach or suggest all the claim limitations, the prior art references, even when combined, leave out the claim limitation of lipooligosaccharide (LOS) of *Moraxella catarrhalis*. Turning next to the first point, that there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference teachings, and even if the prior art references included the missing claim limitation, there is no suggestion or motivation to modify the reference teachings. This is because the references point to outer membrane proteins of *Moraxella catarrhalis*, like UsPA and CD, for use as vaccines, especially because, as taught by Murphy, col. 2, LOS is unacceptable due to its toxicity, and Hu et al., Infection and Immunity, vol. 68, No. 9, pp. 4980-4985, Sept 2000, at p. 4980, col. 2, 1st full sentence, attached, reports that these outer membrane proteins were already being developed as successful vaccines.

Finally, reaching the last point, that there must be a reasonable expectation of success, according to Hu et al., Infection and Immunity, vol. 68, No. 9, pp. 4980-4985, Sept 2000, at p. 4980, col. 2, 2nd full sentence, attached, formerly there was no vaccine available to prevent the diseases caused by *Moraxella catarrhalis*, largely because the pathogenic mechanism and the host immune response to this pathogen had yet to be clarified. In view of Erwin et al, Infection and Immunity, Vol. 59, No. 6, pp. 1881-1887, June 1991, at abstract, last line, page 1884, col 2, line 12, and page 1886, col 1, line 13, attached, it would not have been reasonable to expect that detoxification of LOS of *Moraxella catarrhalis* to produce dLOS or OS would retain its antigenicity sufficient to produce antibodies having bactericidal activity against *Moraxella catarrhalis*. Yet Example 6, beginning at page 35, first paragraph, and Example 11, beginning at page 45, last paragraph, evidence bactericidal activity of antibodies produced upon immunization with dLOS and OS against *Moraxella catarrhalis*. Thus, at the time of the invention, there was an element of unpredictability as to whether a LOS of *Moraxella catarrhalis* detoxified to produce dLOS or OS would be antigenic. Antigenicity has to be

determined on a preparation by preparation basis. The admission by Erwin et al negates any reasonable expectation of successfully doing what the inventors now claim. *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (Obviousness under §103 requires "a reasonable expectation of success.")

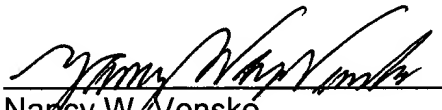
CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 12/19/01

By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

On this set of pages, the insertions are double underlined while the ~~deletions are struck through~~.

1. (Amended) An immunogenic composition ~~A conjugate vaccine for *Moraxella catarrhalis*~~, comprising a lipooligosaccharide (LOS) isolated from *Moraxella catarrhalis* ~~*M. catarrhalis*~~ and detoxified by treating to remove esterified fatty acids to produce detoxified LOS (dLOS), or by treating to remove lipid A to produce oligosaccharide (OS), and an immunogenic carrier covalently linked thereto.

2. (Amended) The immunogenic composition ~~vaccine~~ of Claim 1, wherein the immunogenic carrier is a protein.

3. (Amended) The immunogenic composition ~~vaccine~~ of Claim 2, wherein the immunogenic carrier protein is selected from the group consisting of UspA isolated from *M. catarrhalis*, CD isolated from *M. catarrhalis*, tetanus toxin/toxoid, a high molecular weight protein (HMP) isolated from nontypeable *Haemophilus influenzae*, diphtheria toxin/toxoid, detoxified *P. aeruginosa* toxin A, cholera toxin/toxoid, pertussis toxin/toxoid, *Clostridium perfringens* exotoxins/toxoid, hepatitis B surface antigen, hepatitis B core antigen, rotavirus VP 7 protein, CRM, CRM_{197}, CRM_{3201} and respiratory syncytial virus F and G protein.

4. (Amended) The immunogenic composition ~~vaccine~~ of Claim 3, wherein the immunogenic carrier protein is tetanus toxoid or HMP.

5. CANCELED

6. (Amended) The immunogenic ~~pharmaceutical~~ composition of Claim 1 ~~Claim 5~~, further comprising an adjuvant.

7. (Amended) The immunogenic ~~pharmaceutical~~ composition of Claim 6, wherein the adjuvant is an admixture of monophosphoryl lipid A and trehalose dimycolate or alum.

8. (Amended) The immunogenic composition of ~~A conjugate vaccine according to~~ Claim 1, wherein the immunogenic carrier is covalently linked to dLOS or to OS via a linker compound.

9. (Amended) The immunogenic composition ~~conjugate vaccine~~ of Claim 8, wherein the linker compound is selected from the group consisting of adipic acid dihydrazide, ε-

aminohexanoic acid, chlorohexanol dimethyl acetal, D-glucuronolactone and p-nitrophenylethyl amine.

10. (Amended) The immunogenic composition ~~conjugate vaccine~~ of Claim 8, wherein the linker compound is adipic acid dihydrazide.

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39. An immunogenic composition comprising a lipooligosaccharide (LOS) isolated from *Moraxella catarrhalis* and detoxified by treating to remove esterified fatty acids to produce detoxified LOS (dLOS) and an immunogenic carrier covalently linked thereto.

40. The immunogenic composition of Claim 39, wherein the immunogenic carrier is a protein.

41. The immunogenic composition of Claim 40, wherein the immunogenic carrier protein is selected from the group consisting of UspA isolated from *M. catarrhalis*, CD isolated from *M. catarrhalis*, tetanus toxin/toxoid, a high molecular weight protein (HMP) isolated from nontypeable *Haemophilus influenzae*, diphtheria toxin/toxoid, detoxified *P. aeruginosa* toxin A, cholera toxin/toxoid, pertussis toxin/toxoid, *Clostridium perfringens* exotoxins/toxoid, hepatitis B surface antigen, hepatitis B core antigen, rotavirus VP 7 protein, CRM, CRM_{197}, CRM_{3201} and respiratory syncytial virus F and G protein.

42. The immunogenic composition of Claim 41, wherein the immunogenic carrier protein is tetanus toxoid or HMP.

43. The immunogenic composition of Claim 39, further comprising an adjuvant.

44. The immunogenic composition of Claim 43, wherein the adjuvant is an admixture of monophosphoryl lipid A and trehalose dimycolate or alum.

45. The immunogenic composition of Claim 39, wherein the immunogenic carrier is covalently linked to dLOS via a linker compound.

46. The immunogenic composition of Claim 45, wherein the linker compound is selected from the group consisting of adipic acid dihydrazide, ε-aminohexanoic acid, chlorohexanol dimethyl acetal, D-glucuronolactone and p-nitrophenylethyl amine.

47. The immunogenic composition of Claim 45, wherein the linker compound is adipic acid dihydrazide.